UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,682	10/29/2003	**Xing Su**	21058/1206739-US1	9817

75172 7590 03/17/2008

Intel Corporation
c/o DARBY & DARBY P.C.
P.O. BOX 770
CHURCH STREET STATION
NEW YORK, NY 10008-0770

EXAMINER	
HA, JULIE	
ART UNIT	**PAPER NUMBER**
1654	

MAIL DATE	DELIVERY MODE
03/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/697,682	SU ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 10-31* is/are pending in the application.

4a) Of the above claim(s) *17-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-16 and 31* is/are rejected.

7)☒ Claim(s) *31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment after Non-final rejection filed on January 02, 2008 is acknowledged. Claim 9 has been cancelled and new claim 31 has been added. Claims 1-8 and 10-31 are pending in this application. Applicant elected Group I(claims 1-16), and because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse. Restriction requirements are deemed proper and made FINAL in the previous office action. Claims 17-30 remain withdrawn from further consideration as being drawn to nonelected inventions. Claims 1-8, 10-16 and 31 are examined on the merits in this office action.

Withdrawn Objection

1. Objection to claims 2-3 are hereby withdrawn due to Applicant's arguments.

Maintained Rejections

35 U.S.C. 112, 2nd

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 2 recites the limitation "template nucleic acid into each chamber" in the second line of the claim. There is insufficient antecedent basis for this limitation in the claim. The template nucleic acid is never mentioned in claim 1. The first time template nucleic acid appears is in claim 2. Claim 1 is drawn to a method of obtaining plurality of labeled proteins, polypeptide or peptides.

Response to Applicant's Arguments

5. Applicant argues that "claim 1 has been amended to recite 'obtaining a plurality of labeled proteins, polypeptides or peptides, and placing the plurality of labeled proteins, polypeptides or peptides in a plurality of chambers, such that different chambers contain a different type of labeled amino acid', thus, there is clear antecedent basis for the chambers in dependent claim 2."

6. Applicant's arguments have been fully considered but have not been found persuasive because claim 1 is drawn to labeled proteins, polypeptides or peptides. Claim 2 is drawn to a template nucleic acid. Claim 1 is drawn to labeled proteins, polypeptides or peptides, not to template nucleic acid, and the nucleic acid appears for the first time in claim 2. Further, it is unclear if only peptides are required to obtain labeled proteins, polypeptides or peptides as in claim 1, or nucleic acid encoding the proteins, polypeptides or peptides are also required, as in claim 2. Therefore, claim 2 lacks antecedent basis for the limitation of "template nucleic acid".

Rejection-35 U.S.C. 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 4-5, 7-8, 10-14, 16 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Chan EY (US Patent # 6210896).

9. The instant claims are drawn to a method comprising a) obtaining one or more labeled proteins, polypeptides or peptides, b) passing the labeled proteins, polypeptides or peptides through one or more nanopores, c) detecting labeled amino acid residues in the labeled proteins, polypeptides or peptides, d) compiling an amino acid distance map for each type of labeled amino acid, and 3) identifying the protein based on the distance maps.

10. Chan EY teaches methods and products for analyzing polymers, and the use of molecular motors to move polymers with respect to a station such that specific signals arise from the interaction between the polymer and an agent at the station (see abstract). The reference teaches the method for analyzing polymers based on the ability to examine each unit of a polymer individually, and by examining each unit individually the type of unit and the position of the unit on the backbone of the polymer can be identified (see column 2, lines 32-38). Furthermore, the reference teaches that one aspect of linear analysis techniques involves the movement of the polymer past a

station in such a manner as to cause a signal that provides information about the polymer to rise (see column 2, lines 52-55). Furthermore, the reference teaches that a method for analyzing a polymer includes the steps of exposing a plurality of individual units of a polymer to an agent selected from the group consisting of an electromagnetic radiation source, a quenching source, and a fluorescence excitation source causing the molecular motor to move the polymer relative to the agent, and detecting signals resulting from an interaction between the units of the polymer and the agent (see column 2, lines 60-67 and column 26). Furthermore, the reference discloses that another preferred method of analysis involves the use of radioactively labeled polymers (see column 27, lines 9-10) and the analysis of the radiolabeled polymers is identical to other means of generating signals (see column 27, lines 47-48). The reference teaches that in one embodiment, the polymer dependent impulses measured is an electromagnetic radiation signal generated, and the units are detected at the signal generation station by measuring light emission at the station, the station can be a nanochannel (see column 6, lines 5-9). The reference further teaches a method for determining the order of units of a polymer of linked units, the method steps includes 1) moving the polymer linearly relative to a station using a molecular motor, 2) measuring a polymer dependent impulse generated as each of two individual units, each giving rise to a characteristic signal, pass by the station, 3) repeat steps 1 and 2, and 4) determining the order of at least the two individual units based upon the information obtained from said plurality of similar polymer (see column 5, lines 54-63). The reference further teaches that the polymer may be any type of polymer of linked

units…nucleic acid or peptide (see column 3, lines 27-32). This reads on claims 1, 5, 7-8, 11-14. The reference further teaches that the labeled polymer is moved linearly relative to a station to produce a characteristic polymer dependent impulse generated as each of the two unit labels passes by the station, and further comprising the step of determining the distance between the polymer dependent impulses as an indication of the distance between the two unit labels (see column 4, lines 35-41). This reads on claims 1, 4, 7-8 and 16. Furthermore, the reference teaches that the method is a method for determining the proximity of two unit labels of the polymer wherein the proximity of the two unit labels is the signature of said polymer dependent impulses, the identity of each unit label being indicative of the identity of at least one unit of the polymer, wherein the labeled polymer is moved relative to a station to expose the two unit labels to the station to expose the two unit labels to the station to produce a characteristic polymer dependent impulse arising from a detectable physical change in the unit label or the station, and further comprising the step of measuring the amount of time elapsed between detecting each characteristic polymer dependent impulse, the amount of time elapsed being indicative of the proximity of the two unit labels (see column 4, lines 42-54). This reads on claim 10. The reference discloses that sequence of polypeptide is determined by comparing the relative mass difference between fragments with the known masses of the amino acid residues (see column 2, lines 8-21). This reads on claim 4. Furthermore, the reference discloses that the ability to determine the distance between two units is important for determining how many units, if any, are between the two units of interest and the sequence of units serves as a

blueprint for a known polymer (see column 13, lines 25-32). The reference teaches that the method is performed on a plurality of polymers, simultaneously (see column 4, lines 8-9). The reference teaches that multiple polymers can be analyzed simultaneously by causing more than one polymer to move relative to respective signal station on respective molecular motors (see column 8, lines 64-66). Furthermore, the reference teaches that FRET analysis can be performed on a single molecule in solution or as parallel reactions on a solid planar medium, or in different solutions, such as in multi-well dishes (see column 9, lines 29-32). Furthermore, the reference discloses analysis of labeled peptide analyzed by nanochannel FRET sequencing. The sequence-specific FRET information arising from each fragment is sorted into one of two complementary strand groups, sorting allows population analysis to determine the positions of all the desired bases, and to thus generate sequence information from the sorted data (see column 21, lines 19-26). Therefore, the reference meets the limitations of claims 1, 4-5, 7-8, 10-14, 16 and 31.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1, 4-5, 7-8, 10-14, 16 and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Chan EY (US Patent # 6355420).

12. The instant claims are drawn to a method comprising a) obtaining one or more labeled proteins, polypeptides or peptides, b) passing the labeled proteins, polypeptides or peptides through one or more nanopores, c) detecting labeled amino acid residues in the labeled proteins, polypeptides or peptides, d) compiling an amino acid distance map for each type of labeled amino acid, and 3) identifying the protein based on the distance maps.

13. Chan EY teaches methods and products for analyzing polymers, and methods for determining various other structural properties of the polymers (see abstract). The reference further teaches that the method for analyzing polymers according to the invention is based on the ability to examine each unit of a polymer individually. By examining each unit individually, the type of unit and the position of the unit on the backbone of the polymer can be identified (see column 6, lines 48-50). Further, an individual unit of the single polymer in one aspect is caused to interact with an agent such that a change, e.g., energy transfer or quenching occurs and produces a signal (see column 7, lines 1-4), and the signal is indicative of the identity of the unit (see column 7, lines 4-5). Furthermore, the reference teaches that the polymer may be any type of polymer known in the art…is selected from the group consisting of a nucleic acid and a protein (see column 8, lines 49-51). The reference discloses that the units of the polymer which interact with the agent to produce a signal are labeled and the units may be intrinsically or extrinsically labeled, and the plurality of individual units of the polymer are exposed to at least two stations positioned in distinct regions of the channel, wherein the interaction between the units of the polymer and two stations produce at

least two signals (see column 8, lines 53-67). The reference teaches that the method includes the steps of transiently moving the individual unit of the polymer relative to a station, the identity of the individual unit being unknown, detecting a signal arising from a detectable physical change in the unit or the station, and distinguishing said signal from signals arising from exposure of adjacent signal generating units of the polymer to the station as an individual unit (see column 10, lines 1-7). Furthermore, the reference discloses that when a unit of the polymer is exposed to the agent, the interaction between the two produces a signal…if each type of unit e.g., each type of amino acid is labeled with a different light emissive compound having a distinct light emissive pattern then each amino acid will interact with the agent to produce a distinct signal. By determining what each signal for each unit of the polymer is, the sequence of units can be determined (see column 27, lines 58-67 and column 28, lines 1-5). Furthermore, the reference discloses that the labeled proteins remain completely stationary in space. By direct analogy, the spatial confinement of the nanochannels should limit or eliminate the Brownian motion of the labeled DNA in nanochannel FRET sequencing. This would allow a stable and predictable passage of the DNA through the nanochannels (see column 35, lines 39-64). The instant specification discloses that the skilled artisan will realize that where the specification refers to a “nanopore” different alternatives may use a “nanochannel” or “nanotube”. The only requirement is that the nanopore, nanochannel or nanotube connect one fluid filled compartment to another and allow the passage and detection of labeled protein (see paragraph [0034]). Thus, this reads on claims 1, 7, 10, 11-13 and 16. The reference further teaches a method for analyzing a polymer of linked

units comprising moving a plurality of individual units of a polymer of linked units through a channel and exposing the plurality of individual units to an agent selected from the group consisting of electromagnetic radiation, a quenching source and a fluorescence excitation source as the units move past the agent, individual units interacting with the agent to produce a detectable signal within the channel or at the edge of the channel (see Claims 1-4). This further reads on claims 7 and 11-14. The reference teaches that the detected signals can be compared to a known pattern of signals characteristic of a known polymer to determine the relatedness of the polymer being analyzed to the known polymer and analysis may also involve measuring the length of time elapsed between detection of a first signal from the first unit and a second signal from a second unit. The time elapsed between the sequential detection of signals may indicate the distance between two units or the length of the polymer (see column 8, lines 36-47). Furthermore, the reference teaches that the method involves the steps of causing the polymer to pass linearly relative to a station, detecting a characteristic signal generated as each of the two individual units passes by the station, measuring the time elapsed between the signals measured, repeating steps for a plurality of similar polymers to produce a data set, and determining the distance between the two individual units based upon the information obtained from the plurality of similar polymers by analyzing the data set. Thus, this meets the limitations of claims 1, 4-5, 7-8, 10-14, 16 and 31.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

14. Claims 1, 4-5, 7-8, 10-14, 16 and 31 are rejected under 35 U.S.C. 102(a) as being anticipated by Chan EY (US Patent # 6355420).

15. The instant claims are drawn to a method comprising a) obtaining one or more labeled proteins, polypeptides or peptides, b) passing the labeled proteins, polypeptides or peptides through one or more nanopores, c) detecting labeled amino acid residues in the labeled proteins, polypeptides or peptides, d) compiling an amino acid distance map for each type of labeled amino acid, and 3) identifying the protein based on the distance maps.

16. Chan EY teaches methods and products for analyzing polymers, and methods for determining various other structural properties of the polymers (see abstract). The reference further teaches that the method for analyzing polymers according to the invention is based on the ability to examine each unit of a polymer individually. By examining each unit individually, the type of unit and the position of the unit on the backbone of the polymer can be identified (see column 6, lines 48-50). Further, an individual unit of the single polymer in one aspect is caused to interact with an agent such that a change, e.g., energy transfer or quenching occurs and produces a signal (see column 7, lines 1-4), and the signal is indicative of the identity of the unit (see column 7, lines 4-5). Furthermore, the reference teaches that the polymer may be any type of polymer known in the art…is selected from the group consisting of a nucleic acid and a protein (see column 8, lines 49-51). The reference discloses that the units of the polymer which interact with the agent to produce a signal are labeled and the units may

be intrinsically or extrinsically labeled, and the plurality of individual units of the polymer are exposed to at least two stations positioned in distinct regions of the channel, wherein the interaction between the units of the polymer and two stations produce at least two signals (see column 8, lines 53-67). The reference teaches that the method includes the steps of transiently moving the individual unit of the polymer relative to a station, the identity of the individual unit being unknown, detecting a signal arising from a detectable physical change in the unit or the station, and distinguishing said signal from signals arising from exposure of adjacent signal generating units of the polymer to the station as an individual unit (see column 10, lines 1-7). Furthermore, the reference discloses that when a unit of the polymer is exposed to the agent, the interaction between the two produces a signal…if each type of unit e.g., each type of amino acid is labeled with a different light emissive compound having a distinct light emissive pattern then each amino acid will interact with the agent to produce a distinct signal. By determining what each signal for each unit of the polymer is, the sequence of units can be determined (see column 27, lines 58-67 and column 28, lines 1-5). Furthermore, the reference discloses that the labeled proteins remain completely stationary in space. By direct analogy, the spatial confinement of the nanochannels should limit or eliminate the Brownian motion of the labeled DNA in nanochannel FRET sequencing. This would allow a stable and predictable passage of the DNA through the nanochannels (see column 35, lines 39-64). The instant specification discloses that the skilled artisan will realize that where the specification refers to a “nanopore” different alternatives may use a “nanochannel” or “nanotube”. The only requirement is that the nanopore, nanochannel

or nanotube connect one fluid filled compartment to another and allow the passage and detection of labeled protein (see paragraph [0034]). Thus, this reads on claims 1, 7, 10, 11-13 and 16. The reference further teaches a method for analyzing a polymer of linked units comprising moving a plurality of individual units of a polymer of linked units through a channel and exposing the plurality of individual units to an agent selected from the group consisting of electromagnetic radiation, a quenching source and a fluorescence excitation source as the units move past the agent, individual units interacting with the agent to produce a detectable signal within the channel or at the edge of the channel (see Claims 1-4). This further reads on claims 7 and 11-14. The reference teaches that the detected signals can be compared to a known pattern of signals characteristic of a known polymer to determine the relatedness of the polymer being analyzed to the known polymer and analysis may also involve measuring the length of time elapsed between detection of a first signal from the first unit and a second signal from a second unit. The time elapsed between the sequential detection of signals may indicate the distance between two units or the length of the polymer (see column 8, lines 36-47). Furthermore, the reference teaches that the method involves the steps of causing the polymer to pass linearly relative to a station, detecting a characteristic signal generated as each of the two individual units passes by the station, measuring the time elapsed between the signals measured, repeating steps for a plurality of similar polymers to produce a data set, and determining the distance between the two individual units based upon the information obtained from the plurality of similar

polymers by analyzing the data set. Thus, this meets the limitations of claims 1, 4-5, 7-8, 10-14, 16 and 31.

Response to Applicant's Arguments

17. Applicant argues that "independent claim 1 has been amended to recite 'obtaining a plurality of labeled proteins, polypeptides or peptides, and placing the plurality of labeled proteins, polypeptides or peptides in a plurality of chambers, such that different chambers contain a different type of labeled amino acid.' Chan does not teach a plurality of labeled proteins, polypeptides or peptides, each placed in a chamber having a different type of labeled amino acid. Therefore, Chan does not anticipate amended claim 1".

18. Applicant's arguments have been fully considered but have not been found persuasive because Chan reference as a whole teaches the claimed invention of instant application. As described above, Chan reference teaches methods and products for analyzing polymers. The reference teaches a method for determining the order of units of a polymer of linked units, determining the order of at least two individual units based upon the information obtained from said plurality of similar polymer (see column 5, lines 54-63). The reference further teaches that the polymer may be any type of polymer of linked units…nucleic acid or peptide (see column 3, lines 27-32). The reference further teaches that when a labeled unit of the polymer is exposed to the agent the interaction between the two produces a signal…if each type of labeled unit e.g., each type of amino acid is labeled with a different light emissive compound having a distinct light emissive pattern then each amino acid will interact with the agent to produce a distinct signal. By

determining what each signal for each labeled unit of the polymer is, the sequence of units can be determined (see column 25, lines 59-60 and column 26, lines 1-4). The reference further teaches that "a plurality of polymers is at least two polymers...in one embodiment is at least 50 polymers...in another embodiment is at least 100 polymers" (see column 13, lines 56-59). The reference teaches that the method is performed on a plurality of polymers, simultaneously (see column 4, lines 8-9). The reference teaches that multiple polymers can be analyzed simultaneously by causing more than one polymer to move relative to respective signal station on respective molecular motors (see column 8, lines 64-66). Furthermore, the reference teaches that FRET analysis can be performed on a single molecule in solution or as parallel reactions on a solid planar medium, or in different solutions, such as in multi-well dishes (see column 9, lines 29-32). Therefore, Chan reference as a whole anticipates the claimed invention of instant application.

Rejection-35 U.S.C. 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

22. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chan EY (US Patent # 6210896) as applied to claims 1, 4-5, 7-8, 10-14, 16 and 31 above.

23. The instant claim is drawn to a method comprising a) obtaining one or more labeled proteins, polypeptides or peptides, b) passing the labeled proteins, polypeptides or peptides through one or more nanopores, c) detecting labeled amino acid residues in the labeled proteins, polypeptides or peptides, d) compiling an amino acid distance map for each type of labeled amino acid, and 3) identifying the protein based on the distance

maps and obtaining one or more proteins, polypeptides or peptides from a biological sample, and labeling the proteins, polypeptide or peptides post-translationally.

24. The teachings of Chan EY are described supra. The difference between the reference and the instant application is that the reference does not teach obtaining one or more proteins, polypeptides or peptides from a biological sample.

25. However, it would have been obvious to one of ordinary skill in the art to try the method of obtaining the identity of the protein of any sample, including proteins from biological samples, by using the teachings of US Patent '896. There is a reasonable expectation of success since the method and the analysis of the Chan patent works on any polymeric compounds, such as DNA, RNA, and proteins that are labeled with luminescent labels, fluorescent labels, phosphorescent labels, chemiluminescent labels…nuclear magnetic resonance labels…electron spin resonance labels…and are detected with a photodetector or with an electrical detector.

26. Claim 2, 6 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan EY (US Patent # 6210896) as applied to claims 1, 4-5, 7-8, 10-14, 16 and 31 above in view of Thompson et al (US Patent # 5324637).

27. The instant claims are drawn to the method of claim 1, further comprising: a) placing a template nucleic acid into at least one chamber, each chamber to contain a different type of labeled amino acid, and b) producing one or more labeled proteins, polypeptides or peptides encoded by the template nucleic acid, and wherein each chamber is operably coupled to a different set of nanopores, and wherein the labeled

amino acids in each chamber represent between about 0.5% and about 50% of the total amount of the same amino acid in that chamber.

28. The teachings of Chan EY are described supra. The difference between the reference and the instant claims are that the reference does not teach nucleic acid into at least one chamber, each chamber containing a different type of labeled amino acid, and producing one or more labeled proteins, polypeptides or peptides encoded by the template nucleic acid, and the amount of labeled amino acid present in each chamber.

29. However, Thompson et al teaches a method for coupling transcription and translation from DNA, wherein RNA is transcribed from DNA and RNA translates into protein (see abstract). The reference further teaches that if a radiolabeled amino acid is used in the coupled reaction, such as ^{35}S methionine or ^{3}H leucine, then the corresponding amino acid is left out of the amino acid mix…RNA polymerase, either SP6, T7 or T3 is then added (see column 8. lines 60-65). Furthermore, the reference teaches that another method of measuring the amount of protein produced in coupled in vitro transcription and translation reactions is to perform the reactions using a known quantity of radiolabeled amino acid such as ^{35}S methionine or ^{3}H leucine and subsequently measuring the amount of radiolabeled amino acid incorporated into the newly translated protein (see column 11, lines 40-46).

30. Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Chan EY patent and Thompson et al patent to obtain the protein identity, because both prior arts teach the identification of proteins, using labeling of the protein such as fluorescence labeling, radiolabeling of proteins (Chan)

and radiolabeling of proteins (Thompson) to quantify and identify the proteins. There is a reasonable expectation of success, since Thompson et al provide a simple method for producing protein from a template DNA, such a method which can be used to couple transcription and translation of a single protein coded by the DNA template (see Thompson et al, column 4, lines 13-20). Furthermore, both prior arts teach radiolabeling of proteins to measure the amounts of labeling and Chan teaches limiting the region of detection of the polymer where the radiolabel exists on the protein.

31. It has been held that under KSR that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in KSR, When there is motivation "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727,_,82 USPQ2d 1385, 1397 (2007).

32. The "problem" facing those in the art was that sequencing polymer methods are slow and labor intensive. For example, Sanger method involves the enzymatic synthesis of DNA molecules terminating in dideoxynucleotides, and subsequent analysis yields information of the length of the DNA molecules and the nucleotide at which each molecule terminates, and thus, the DNA sequence can be determined. The other method is Maxam and Gilbert method, which uses chemical degradation to generate a population of molecules degraded at certain positions of the target DNA, and with

knowledge of the cleavage specificities of the chemical reactions and the lengths of the fragments, the NDA sequence is generated (see Chan patent '896, column 1, lines 32-47) and each process takes about 1-3 days, and there were a limited number of methodologies available to do so, for example radiolabeling the protein sequence, DNA sequencing, mass spectroscopy and ELIDA sequencing. The skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. In this case, Chan patent teaches that any polymer sequence can be labeled and run through the nanochannel, and the distance of each polymeric sequence can be read separately, for any DNA and protein sequences. Thus, performing a transcription coupled translation a radiolabeling the protein that is translated from RNA is a "the product not of innovation but of ordinary skill and common sense," leading to the conclusion that invention is not patentable as it would have been obvious.

Response to Applicant's Arguments

33. Applicant argues that "the features of 'placing plurality of labeled proteins, polypeptides or peptides in a plurality of chambers, such that different chambers contain a different type of labeled amino acid' is neither taught nor suggested by any of the applied references." Furthermore, Applicant argues that "Thompson does not teach a plurality of chambers each having a different type of labeled amino acid. Therefore, the combination of Chan and Thompson does not teach all of the features of the claimed invention."

34. Applicant's arguments have been fully considered but have not been found persuasive because as described above, Chan reference as a whole teaches the limitations of instant claims. As described above in the rejection, Thompson reference teaches that another method of measuring the amount of protein produced in coupled in vitro transcription and translation reactions is to perform the reactions using a known quantity of radiolabeled amino acid such as ^{35}S methionine or ^{3}H leucine and subsequently measuring the amount of radiolabeled amino acid incorporated into the newly translated protein (see column 11, lines 40-46). Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Chan EY patent and Thompson et al patent to obtain the protein identity, because both prior arts teach the identification of proteins, using labeling of the protein such as fluorescence labeling, radiolabeling of proteins (Chan) and radiolabeling of proteins (Thompson) to quantify and identify the proteins. There is a reasonable expectation of success, since Thompson et al provide a simple method for producing protein from a template DNA, such a method which can be used to couple transcription and translation of a single protein coded by the DNA template. As described in the KSR analysis, sequencing polymer methods are slow and labor intensive, each process taking about 1-3 days, and there were a limited number of methodologies available to do so, for example radiolabeling the protein sequence, DNA sequencing, mass spectroscopy and ELIDA sequencing. The skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. In this case, Chan patent teaches that any polymer sequence or plurality of polymer sequences in multi-

well can be labeled and run through the nanochannel, and the distance of each polymeric sequence can be read separately, for any DNA and protein sequences. Thus, performing a transcription coupled translation a radiolabeling the protein that is translated from RNA is a "the product not of innovation but of ordinary skill and common sense," leading to the conclusion that invention is not patentable as it would have been obvious. Therefore, the prior arts are prima facie obvious.

New Objections

35. Claim 31 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 31 recites, "wherein each chamber contains a different type of labeled amino acid". Claim 1, 4th line recites, "different chambers contain a different type of labeled amino acid". The two claims are worded differently, but the claims cover the same thing.

Conclusion

36. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action. No claims are allowed.

37. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Julie Ha/
Examiner, Art Unit 1654

/Anish Gupta/
Primary Examiner, Art Unit 1654